



Non-invasive ventilation 2

Ventilatory support after extubation in critically ill patients

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This is the second in a Series of two papers about non-invasive ventilation

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The **periextubation** period represents a crucial moment in the management of critically ill patients. **Extubation failure**, defined as the need for **reintubation within 2–7 days after a planned extubation**, is associated with **prolonged mechanical ventilation, increased incidence of ventilator-associated pneumonia, longer intensive care unit and hospital stays, and increased mortality**. Conventional oxygen therapy is commonly used after extubation. Additional methods of non-invasive respiratory support, such as **non-invasive ventilation and high-flow nasal therapy**, can be used to **avoid reintubation**. The aim of this Review is to describe the pathophysiological mechanisms of postextubation respiratory failure and the available techniques and strategies of respiratory support to avoid reintubation. We summarise and discuss the available evidence supporting the use of these strategies to achieve a tailored therapy for an individual patient at the bedside.

Introduction

The peri-extubation period represents a crucial moment in the management of critically ill patients. **Postextubation acute respiratory failure (ARF)** occurs in **10–20%** of patients who meet all weaning criteria and successfully perform a **spontaneous breathing trial**, who might require **emergency reintubation**.^{1,2} Reintubation is usually related to airway failure (aspiration, ineffective cough, or upper airway obstruction), weaning failure (primary respiratory failure, congestive heart failure, onset of new sepsis, acute coronary syndrome, or neurological impairment), or surgical complications such as bleeding or anastomotic leak.³ In particular, **surgical complications** are a major cause of extubation failure in the **postoperative** setting, needing prompt identification and correction.

Extubation failure has been defined as the need for **reintubation occurring within 2–7 days after a planned**

extubation,^{1,3} resulting in **increased mortality (25–50%)**, **prolonged mechanical ventilation, increased frequency of ventilator-associated pneumonia**, and longer intensive care unit (ICU) and hospital stays.^{4–7} It is therefore essential to identify patients at high risk of postextubation ARF in order to choose an appropriate strategy of respiratory support able to improve their outcome.

Conventional oxygen therapy (COT) is commonly used to correct residual oxygenation impairment after extubation, a condition reported as a frequent cause of weaning failure.^{8,9} Although **COT can improve oxygenation**, it has only a **minimal effect on the main pathophysiological mechanisms** which can lead to postextubation ARF and reintubation (eg, **atelectasis, excessively high respiratory workload, or decreased respiratory muscle force**). Non-invasive ventilation (NIV) and high-flow nasal therapy (HFNT) have been implemented as **effective alternative approaches aimed at protecting extubation**.^{10–12}

In this Review we will describe the pathophysiological mechanisms of postextubation ARF, the main techniques of non-invasive respiratory support used after extubation (NIV, HFNT, and COT), strategies of postextubation respiratory support (facilitative, preventive, and therapeutic) and their indications to achieve a tailored therapy for specific types of patient, and areas of uncertainty and of future research.

Pathophysiological changes related to extubation

Extubation and the subsequent passage from positive pressure mechanical ventilation to unassisted breathing are the cause of several pathophysiological changes in the airway status or in the weaning (cardiorespiratory) status, including lung aeration, haemodynamics, and neuromuscular function, which, alone or in association, are the substrate for extubation failure, especially in high-risk patients (figure 1).

Changes in airway status

Upper airway obstruction is one of the **common** causes of extubation failure (**2–16%** of ICU patients), requiring, in

Key messages

- **Extubation failure** is associated with prolonged mechanical ventilation, increased frequency of ventilator-associated pneumonia, longer stays in the intensive care unit and in the hospital, and increased mortality
- **Identifying** patients at greater risk of extubation failure is important for choosing the appropriate technique of non-invasive ventilatory support to improve weaning outcome
- Several techniques of respiratory support (conventional oxygen therapy, high-flow nasal therapy, continuous positive airway pressure, and non-invasive ventilation) can be used with different strategies (facilitative, preventive, or therapeutic) to avoid extubation failure
- Any **postextubation respiratory support** treatment should **not delay intubation** and escalation to invasive mechanical ventilation, when this is more appropriate
- In the era of precision medicine and personalisation of care, future studies are needed to help clinicians to use the right device, with the right setting, in the right patient, at the right time

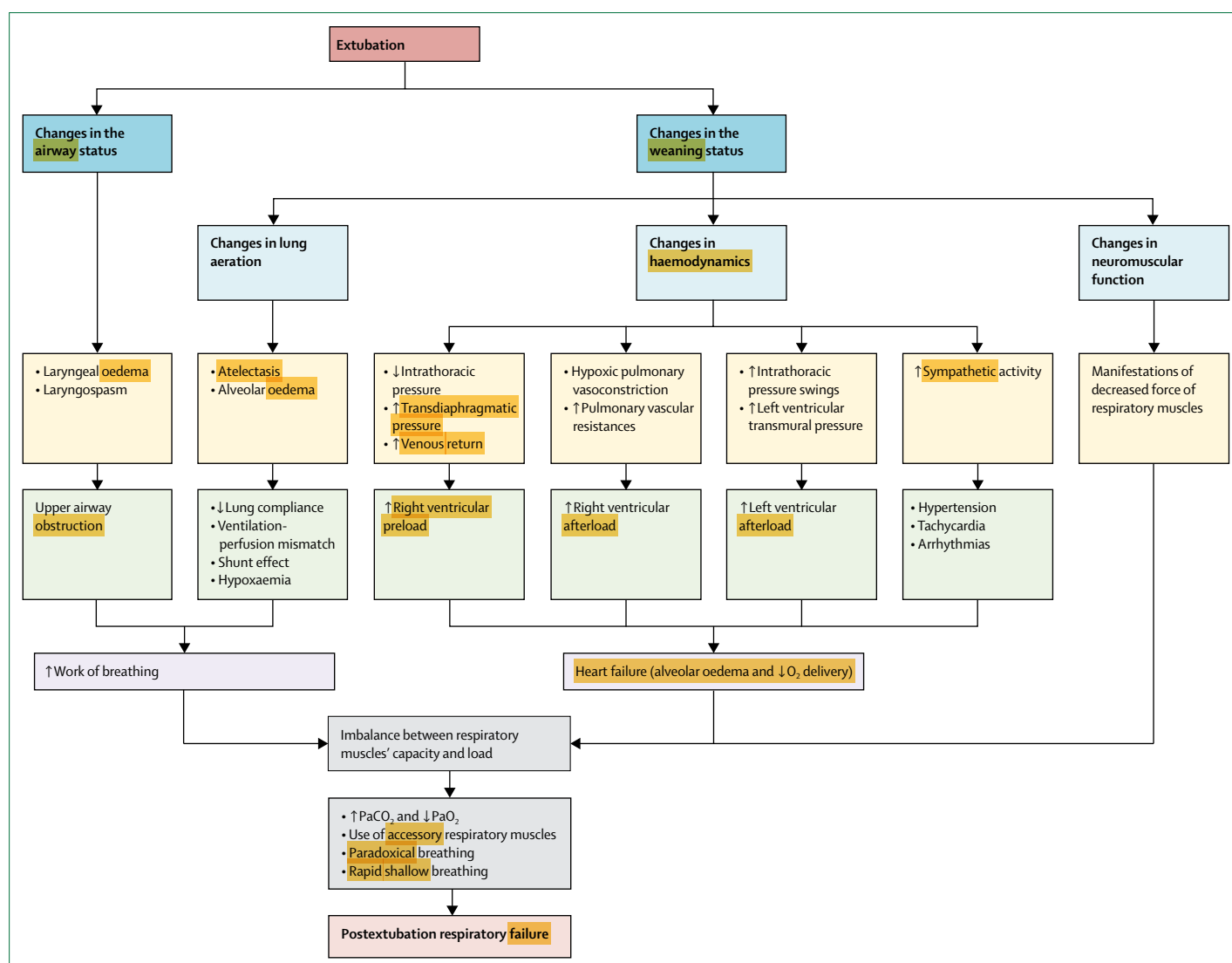


Figure 1: Pathophysiological changes in the airway and weaning status occurring after extubation and their linkage with postextubation respiratory failure

PaO₂=arterial partial pressure of oxygen. PaCO₂=arterial partial pressure of blood carbon dioxide.

some cases, an emergent reintubation.¹³ The most frequent cause of upper airway obstruction after extubation is laryngeal oedema, which derives from mechanical trauma caused by the intubation, especially in cases of difficult intubation, multiple intubation attempts, prolonged intubation, use of inappropriately large endotracheal tube size, high cuff pressure, female sex, and reintubation after unplanned extubation. After removal of the endotracheal tube, the airway diameter might be substantially reduced, thus increasing airway resistance, which, in turn, can lead to respiratory distress.¹³⁻¹⁵ The quantitative cuff leak test is a screening test recommended before extubation in patients at risk of postextubation stridor.¹⁶ The test is considered positive when the cuff leak volume (which is the difference between expiratory volume with inflated cuff and expiratory volume when the cuff is deflated) is less than

130 mL or if the expiratory volume with deflated cuff is less than 12% of the inspiratory volume. In these cases, the administration of steroids, at least 4 h before extubation, might decrease laryngeal inflammation and oedema.^{12,13,17} Another less frequent cause of upper airway obstruction is represented by laryngospasm due to a greater susceptibility of inflamed airway to reflexogenic stimuli, such as epipharyngeal and laryngopharyngeal stimulation.

Additionally, excessive tracheobronchial secretions at the time of extubation, together with a weak or ineffective cough, can lead to impaired airway competency and, consequently, to extubation failure.

Changes in weaning status

Weaning status includes lung aeration, haemodynamics, and neuromuscular function. Discontinuation of

mechanical ventilation might cause a loss of pulmonary aeration, leading to decreased lung compliance, ventilation–perfusion mismatch, and shunt effect.^{18,19} Different pathophysiological changes are associated with loss of lung aeration, such as atelectasis, alveolar transudation, and oedema. During spontaneous breathing, the decrease in transpulmonary end-expiratory pressure can reduce lung volume to values below the closing capacity in unstable alveoli, resulting in collapse and atelectasis formation. Atelectasis plays a fundamental role in the pathophysiology of postextubation ARF because the heterogeneity of the lung parenchyma can lead to elevated regional driving transpulmonary pressure (the difference between end-inspiratory transpulmonary pressure and end-expiratory transpulmonary pressure), worsening of lung injury, pulmonary oedema, and respiratory distress.^{18,19} Besides, intrapulmonary shunt in atelectatic zones elicits hypoxic pulmonary vasoconstriction, which increases pulmonary vascular resistances. Alveolar transudation and oedema after extubation are caused by increased difference between intravascular capillary pressure and alveolar pressure and by increased cardiac output.

Discontinuation of mechanical ventilation can cause pronounced negative swings in intrathoracic pressure, depending on the patient's inspiratory effort.^{18–21} This implies an increase in left ventricular transmural pressure and afterload, which derives from the difference between systolic aortic pressure and intrathoracic pressure. Transdiaphragmatic pressure (the difference between abdominal pressure and intrathoracic pressure) increases after discontinuation of ventilation because there is a greater diaphragmatic excursion during spontaneous breathing than during mechanical ventilation, causing higher abdominal pressure and a compressive effect on the abdominal viscera and vessels, while intrathoracic pressure decreases to negative values. This pressure gradient leads to an increase in venous return and in right ventricular preload. In addition, at extubation, stimulation of airway receptors causes increased sympathetic activity, which might result in hypertension, increased heart rate, and arrhythmias.^{22,23}

Liberation from mechanical ventilation requires adequate neuromuscular activity to overcome the impedance of the respiratory system, to meet metabolic demands, and to maintain adequate gas exchanges.¹ Mechanical ventilation can be associated with diaphragmatic weakness, injury, and atrophy, which occur rapidly in critically ill patients, leading to difficult weaning.²⁴ Diaphragmatic atrophy is associated with excessive ventilatory assistance, which acts on central drive to suppress the patient's inspiratory effort, whereas inadequate ventilatory support potentially causes insufficient unloading of the respiratory muscles, leading to load-induced diaphragmatic inflammation and injury.²⁵ Other risk factors are related to diaphragmatic dysfunction in critically ill patients, such as primary neuromuscular weakness and critical illness polyneuropathy and

myopathy.²⁶ Several studies have shown that diaphragm dysfunction developing during mechanical ventilation is strongly linked to difficult weaning and worsened clinical outcomes.^{25,27–29} During unassisted breathing after extubation, these changes in diaphragm function can lead to an imbalance between the respiratory muscles' capacity and the respiratory load, with clinical manifestations of respiratory distress such as use of accessory respiratory muscles, paradoxical breathing, rapid shallow breathing, and gas exchange impairment.

All these pathophysiological changes can lead to increased work of breathing and CO₂ production, worsening of oxygenation, recruitment of accessory respiratory muscle, paradoxical breathing, rapid-shallow breathing and, thus, a further increase in respiratory load. The imbalance between the available respiratory muscle force and the required muscle power finally results in muscle exhaustion and ARF. Furthermore, hypoxia and metabolic acidosis impair respiratory muscle function and cardiac function, triggering a vicious circle that, in the absence of adequate therapeutic measures, can lead to cardiorespiratory arrest.

Techniques of respiratory support after extubation

Different techniques, such as NIV, HFNT, or COT, are used to support oxygenation or spontaneous ventilation with the aim of protecting extubation. We summarise the main physiological effects of each technique, focusing on the relevant aspects in the postextubation setting.

Non-invasive ventilation

NIV is a form of mechanical ventilatory support that does not require an artificial airway (endotracheal tube or tracheostomy) and is provided through various interfaces (ie, mask, helmet, prongs).³⁰ The term NIV usually includes both continuous positive airway pressure (CPAP) and non-invasive, bi-level positive pressure ventilation, often delivered with pressure support ventilation and positive end-expiratory pressure.³¹ In this Review, we use the term NIV to refer to bi-level positive pressure ventilation, and use the term CPAP to specifically refer to this distinct mode. CPAP delivers a constant positive airway pressure throughout the entire respiratory cycle (both inspiration and expiration), without providing any assistance to the patient's inspiratory effort. NIV is a ventilatory technique in which a positive inspiratory pressure (ie, pressure support ventilation) is provided by the ventilator, assisting the patient's inspiratory effort.^{21,30}

In patients without criteria for immediate intubation (eg, inability to protect the airways, cardiorespiratory arrest), NIV offers several advantages compared with invasive mechanical ventilation, including improved patient comfort, reduced sedation need, lower frequency of nosocomial infections, and fewer complications related to the intubation manoeuvre (eg, airway injuries, laryngeal oedema, and glottic oedema).^{32–36}

NIV and CPAP have several physiological effects on the respiratory and cardiovascular systems. CPAP and HFNT are described, underlining how it is a technique of true positive end-expiratory pressure prevent airway closure respiratory support, rather than an alternative way to and alveolar collapse at the end of expiration, thus simply deliver oxygen therapy.^{49,50-55} First, HFNT is able to promoting alveolar recruitment, increasing aerated lung deliver a higher and more stable \dot{V}_O . The continuous, volume, decreasing ventilation-perfusion mismatch, high gas flow, in fact, can match or even exceed the patient's and improving hypoxaemia.²¹ Application of a pressure inspiratory flow, thus decreasing entrainment of ambient above positive end-expiratory pressure (ie, in pressure air during inspiration and improving oxygenation.^{49,55-59} support ventilation mode) supports the inspiratory phase. Second, the high gas flow washes out the upper airway and increases tidal volume and alveolar ventilation, (anatomic) dead space. In a study in ten healthy volunteers, leading to an improvement in gas exchange.^{36,37} NIV also Moller and colleagues³⁸ showed a direct relationship reduces the work of breathing. The inspiratory pressure between gas flow rate and clearance of a radioactive tracer support decreases indices of diaphragmatic effort and gas in the upper airways, confirming their previous energy expenditure (eg, transdiaphragmatic pressure findings in an upper airway model.⁶¹ In three tracheotomised and pressure-time product, diaphragmatic electric patients, these authors reported flow-dependent \dot{V}_O activity).^{36,37} The use of positive end-expiratory pressure increase and reduced inspired carbon dioxide (\dot{V}_O) on the further reduces the work of breathing by decreasing trachea, which supports the hypothesis that HFNT inspiratory threshold load (in patients with intrinsic decreases rebreathing and dead space, thus improving positive end-expiratory pressure) and elastic load by alveolar ventilation and gas exchange. Third, HFNT increasing respiratory system compliance.³⁸⁻⁴¹ The generates positive airway pressure. The high gas flow change in respiratory pattern and reduction of dyspnoea increases expiratory resistance, thus raising upper airway are important clinical effects resulting from gas pressure during expiration (positive end-expiratory exchange improvement and from reduction of the pressure effect).⁵⁴ This effect is dependent on gas flow, patient's inspiratory effort.^{36,37} Compared with spontaneous mouth opening, and size of the nasal cannula. Studies have taneous breathing, positive pressure ventilation delivered shown a positive linear correlation between the set gas flow during NIV and CPAP reduces left ventricular preload, and the value of mean airway pressure,⁶² which can reach afterload, and compliance in healthy individuals,^{21,42,43} an average of 3 cm H₂O (SD 1) at 50 L/min when the These effects can be useful in pathological conditions, mouth is closed.⁶² The higher airway pressure increases the such as ARF owing to cardiogenic pulmonary oedema end-expiratory lung volume, promoting alveolar and heart failure, a not-infrequent condition associated recruitment and preventing alveolar collapse, which with extubation occurring as a consequence of the improves ventilation:perfusion ratio and oxygenation.^{54,55,63} change in intrathoracic pressure (from positive during Another physiological effect of the HFNT is to decrease mechanical ventilation to negative after extubation) in the patient's inspiratory effort. In a physiological study in patients with heart disease (eg, coronary artery disease or patients with acute respiratory failure, Mauri and colleagues mitral valve disease). In this case, the constant positive reported that, as compared with a standard facial mask, pressure provided throughout the respiratory cycle with HFNT decreased oesophageal pressure swings (by 19% on CPAP increases intrathoracic pressure, reduces venous average) and pressure-time product, a measure of the return to the right atrium, and decreases left ventricular metabolic work of breathing (by 28% on average). Several transmural pressure (and, accordingly, left ventricular mechanisms might explain the reduction in the patient's afterload), thus resulting in enhanced left ventricular inspiratory effort with HFNT, including the decrease in performance and decreased extravascular lung water. hypoxic drive related to improvement in oxygenation, Several studies have shown that, as compared with CO₂ enhanced CO₂ clearance related to washout of the upper the application of CPAP and NIV in patients with airways, and improvement in lung mechanics. In addition, cardiogenic pulmonary oedema has many beneficial the high gas flow splints the upper airways, reducing their physiological effects, including improvement in tendency to collapse. This causes a reduction of inspiratory respiratory mechanics and gas exchange, decrease in airway resistance and a lower resistive respiratory work. work of breathing, and reduction of systolic arterial. Finally, HFNT improves humidification of inspired gas, pressure and heart rate,⁴⁵ which can decrease the need facilitating clearance of secretions through preservation of normal ciliary function of epithelial cells and composition of mucus.^{52,64} Moreover, delivery of heated and humidified gas decreases the metabolic cost of breathing associated with gas conditioning.

High-flow nasal therapy

Clinical efficacy of HFNT is already known in the neonatal and paediatric settings⁵, but in recent years HFNT has been increasingly used in critically ill adults.⁵ This device delivers high flow of humidified gas, with a set inspired oxygen fraction (F_IO₂) and a set gas flow up to 100 L/min (most commonly 50–60 L/min).⁹

All these effects contribute to improve patient comfort and alleviate dyspnoea during HFNT.⁵⁷ As compared with other forms of oxygen therapy and respiratory support delivered through a facial interface, the greater comfort with HFNT is also related to the nasal interface, which

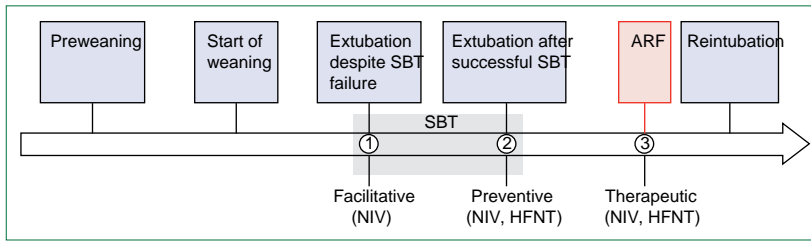


Figure 2: Strategies of ventilatory support after extubation. SBT=spontaneous breathing trial. ARF=acute respiratory failure. NIV=non-invasive ventilation. HFNT=high-flow nasal therapy.

	Facilitative	Preventive	Therapeutic
NIV–CPAP*	Suggested in patients with hypercapnic respiratory failure; no recommendation for hypoxaemic patients	Not suggested in non-high-risk medical patients; suggested for postoperative acute respiratory failure	Not suggested in patients with established postextubation respiratory failure; suggested for patients with postoperative acute respiratory failure
HFNT	No data available in medical patients	Better than COT in unselected, non-high-risk medical patients; similar to NIV in high-risk medical patients; at least non-inferior to NIV in patients at risk of postoperative ARF after cardiothoracic surgery	No data available in medical patients; non-inferior to NIV in patients with postoperative cardiothoracic surgery

NIV=non-invasive ventilation. CPAP=continuous positive airway pressure. HFNT=high-flow nasal therapy. COT=conventional oxygen therapy. ARF=acute respiratory failure. *Based on the official ERS–ATS clinical practice guidelines on NIV for ARF and the ATS–ACCP clinical practice guidelines on liberation from mechanical ventilation in critically ill adults.¹²

Table 2: Strategies of postextubation ventilatory support

Ventilatory strategies to protect extubation in different patient populations

Libertating a patient from invasive mechanical ventilation is a daily challenge in the ICU. The planned extubation is a crucial moment whose timing is determined by resolution of the underlying cause of ARF and a successful spontaneous breathing trial. Even if the spontaneous breathing trial is successful, extubation can fail and might result in reintubation. Reintubation is associated with a greater risk of unfavourable outcome, leading to prolonged mechanical ventilation, a higher risk of ventilator-associated pneumonia, longer ICU and hospital stays, and increased mortality. Implementing an appropriate strategy of postextubation ventilatory support can improve outcome.

Three strategies of ventilatory support can be used after extubation: facilitative, when it allows an early extubation in selected patients who have failed the spontaneous breathing trial, with the aim of reducing duration of invasive ventilation and its associated complications; preventive, in selected and unselected patients, to prevent onset of postextubation ARF; and therapeutic, to avoid reintubation in patients with postextubation ARF (figure 2, table 1).

Facilitative strategy

Patients who have difficult weaning are exposed to complications related to prolonged invasive mechanical ventilation. In these patients, duration of the weaning phase can exceed 40–50% of the overall ventilation period. Patients at higher risk of weaning failure often have been admitted with acute exacerbations of COPD, develop hypercapnia during the spontaneous breathing trial, or both. When these patients fail to meet extubation criteria after the spontaneous breathing trial, non-invasive ventilatory strategies for facilitative purpose allow early extubation, a shorter duration of invasive mechanical ventilation, and a faster weaning process. NIV is the only therapy in the hospital setting. Supplemental oxygen therapy is prescribed to correct hypoxaemia and to prevent tissue hypoxia, preventing a switch to anaerobic metabolism, lactic acidosis, and ultimately cellular damage. COT is provided by easy-to-use devices, which are divided into low-flow devices (eg, nasal cannulae and simple face masks, with or without reservoirs) and high-flow devices (eg, the Venturi mask). Low-flow nasal that pressure support ventilation, delivered during invasive cannulas can be used at a maximum set flow of ventilation (before extubation) and during NIV (after extubation), produced the same effects in terms of gas exchange, diaphragmatic effort, and respiratory mechanics.³² Furthermore, the dyspnoea score was substantially lower during NIV. The first clinical study on facilitative use of NIV during weaning was done by Nava and colleagues in 50 patients with COPD and hypercapnic ARF, who were invasively ventilated for 48 h and had experienced failure of the first spontaneous breathing trial. These authors reported that early, continuous NIV, applied just after extubation as a bridge to unsupported spontaneous breathing, was able to reduce duration of mechanical

does not interfere with normal daily activities and results in higher compliance with treatment even in patients with claustrophobia who are intolerant to other devices.^{65,66}

Oxygen

Oxygen is one of the most frequently administered therapies in the hospital setting. Supplemental oxygen therapy is prescribed to correct hypoxaemia and to prevent tissue hypoxia, preventing a switch to anaerobic metabolism, lactic acidosis, and ultimately cellular damage. COT is provided by easy-to-use devices, which are divided into low-flow devices (eg, nasal cannulae and simple face masks, with or without reservoirs) and high-flow devices (eg, the Venturi mask). Low-flow nasal that pressure support ventilation, delivered during invasive cannulas can be used at a maximum set flow of ventilation (before extubation) and during NIV (after extubation), produced the same effects in terms of gas exchange, diaphragmatic effort, and respiratory mechanics.³² Furthermore, the dyspnoea score was substantially lower during NIV. The first clinical study on facilitative use of NIV during weaning was done by Nava and colleagues in 50 patients with COPD and hypercapnic ARF, who were invasively ventilated for 48 h and had experienced failure of the first spontaneous breathing trial. These authors reported that early, continuous NIV, applied just after extubation as a bridge to unsupported spontaneous breathing, was able to reduce duration of mechanical

ventilation, ICU length of stay, ventilator-associated pneumonia, and 60-day mortality, as compared with facilitate weaning from mechanical ventilation in conventional weaning done with invasive ventilation. In patients with hypercapnic ARF (conditional recommendation, moderate certainty of evidence), whereas no studies have assessed the effect of HFNT to facilitate weaning success, survival, and ICU length of stay. NIV weaning from mechanical ventilation. A post-hoc analysis⁹ of the Bilevel Positive Airway Pressure Versus Optiow study⁹⁰ suggested that facilitative HFNT or NIV increased. Similar results were found in a subsequent, larger randomised controlled trial. The clinical benefits of patients who underwent cardiothoracic surgery (28% for facilitative use of NIV were further supported in a small HFNT vs 41% for NIV, respectively, $p=0.33$), but too few randomised controlled trial in patients with persistent patients were included for any meaningful conclusion on weaning failure (ie, for 3 days). The trial was stopped after this issue.

the first planned interim analysis (33 patients enrolled)

because the NIV group showed a substantial reduction in Preventive strategy

duration of invasive ventilation, nosocomial acquired Respiratory support after extubation for preventive infections, tracheotomy, ICU stay, mortality, and other purposes aims to avoid postextubation ARF in patients serious complications. Burns and colleagues^{5,77} have done undergoing planned extubation. Identifying patients at several systematic reviews and meta-analyses, the last risk is important to select the most appropriate technique which included 16 randomised controlled trials for a total of respiratory support and to prevent extubation failure. 994 patients, invasively ventilated for ARF from different Various risk factors for extubation failure have been causes (COPD, non-COPD, postoperative, medical) and described in the literature. They can be classified as risk weaned by means of early extubation followed by factors related to the patient or comorbidities, risk factors immediate application of NIV or invasive weaning. Most related to acute pathology, and risk factors related to included patients had COPD exacerbations, eight functional parameters, such as bedside predictive tests included COPD exacerbations only, seven included a mixed panel)^{1,3,4,7,81-88} The most commonly reported risk factors (but mostly COPD exacerbation), and one included are older age (>65 years) and underlying cardiac hypoxaemic patients. They found that, compared with or respiratory disease.¹¹ The patient's category (ie, medical invasive weaning, weaning with NIV substantially or surgical) is also important, with extubation failure being decreased mortality, with greater benefits only in patients more prevalent in critically ill medical patients (up to more with COPD (risk ratio [RR] 0.36, 95% CI 0.24-0.56 in than 20%) than in a surgical, postoperative setting (<10%). COPD vs RR 0.81, 95% CI 0.47-1.40 in mixed population).

Furthermore, patients who received NIV had substantially Critically ill medical patients

shorter ICU stays, hospital stays, duration of invasive The effects of early application of NIV and HFNT soon mechanical ventilation, and total duration of ventilation, after extubation, as an alternative to COT, have been and substantially less frequent weaning failure, ventilator-assessed in unselected, non-high-risk patients (ie, any associated pneumonia, tracheotomy, and reintubation. patients without risk factors after planned extubation) Interpretation of these results should, however, take into and in high-risk patients.

account the limitations of the studies, which are mainly In unselected, non-high-risk patients, two studies did due to poor generalisability to different patient categories not show differences between preventive NIV and COT and the small number of patients included in each study.⁷ on reintubation frequency and mortality.^{34,91} On the basis One pilot trial (the one trial of hypoxaemia included in the of these data, the ERS-ATS guidelines suggested not to Burns meta-analysis) has assessed the effects of NIV as a use NIV to prevent postextubation ARF in this setting facilitative strategy for weaning in patients with hypoxaemic (conditional recommendation, very low certainty of ARF.⁷⁸ After 48 h of invasive ventilation, 20 hypoxaemic evidence)¹

patients were randomly assigned to standard weaning or to Studies have highlighted the role of HFNT to prevent early extubation and NIV. There were no differences in gas postextubation ARF. Maggiore and colleagues⁸² did an exchange and likelihood of weaning success, but the open-label, bi-centre, randomised controlled trial to number of days of invasive ventilation were substantially compare the effects of HFNT and COT (through a reduced in the NIV group. Although these results suggest Venturi mask) applied immediately after extubation in the feasibility of facilitative NIV in selected hypoxaemic 105 critically ill patients with moderate hypoxaemia (ie, patients at experienced centres, the small number of arterial partial pressure of oxygen [PaO_2]/ P_{aO_2} 300) at patients precludes the drawing of any meaningful the end of the spontaneous breathing trial preceding conclusion. extubation. For the same delivered P_{aO_2} , patients treated

On the basis of the available evidence, the European with HFNT showed better oxygenation than those treated Respiratory Society (ERS) and American Thoracic with the Venturi mask and this effect lasted up to 48 h.

Panel: Risk factors for extubation failure

Factors related to patient and comorbidities

- Age >65 years⁸⁵
- Moderate or severe cardiorespiratory disease
- Body-mass index ≥ 30

Factors related to acute pathology

- Neurological disease
- Airway patency problem
- Inability to deal with respiratory secretions
- APACHE II >12 on extubation day
- Difficult or prolonged weaning
- ARF of cardiac origin
- Pneumonia as the reason for intubation
- Positive fluid balance

Factors related to functional parameters

- Respiratory rate >35 breaths/min
- Rapid shallow breathing index ≥ 105
- MIP > 20 to 25 cm H₂O⁸²
- Peak expiratory flow <60 L/min
- P_{0.1} 4-5 cm H₂O⁸²
- VC 10 mL/kg⁸²
- P_{0.1}/MIP <0.3

APACHE II=Acute Physiologic Assessment and Chronic Health Evaluation II. ARF=acute respiratory failure. MIP=maximum inspiratory pressure by occlusion pressure at 0.1 s. VC=vital capacity.

Patients receiving HFNT also showed a reduction in ARF.⁸⁴ A reduction in postextubation ARF (16% for NIV vs 33% for COT, $p=0.03$) and in ICU mortality (3% vs 14%, $p=0.015$) was statistically significant at 3 h after extubation. In addition, patients experienced less mortality and 90-day survival were similar. In patients with discomfort, fewer displacements of the interface, and fewer desaturations with HFNT. Finally, fewer patients had postextubation ARF requiring any form of ventilator support (8% for HFNT vs 35% for Venturi mask, $p<0.001$), NIV (4% vs 15%, $p=0.042$), or reintubation (4% vs 21%, $p=0.005$) in the HFNT group, suggesting a potential role of this technique in preventing extubation failure. The benefit of HFNT in reducing reintubation failure. The benefit of HFNT in reducing reintubation failure was observed mainly in patients reintubated because of hypoxaemia or inability to clear secretions.⁸⁵ Hernández and colleagues did a multicentre randomised controlled trial to assess the effects of 24 h of HFNT and COT in 527 mechanically ventilated patients (medical and surgical) at low risk for extubation (23 [15%] of 150 patients in the HFNT group vs 23 [28%] of 83 in the control group).⁸⁹ In line with the results of Maggiore and colleagues,⁸⁸ they found that use of HFNT was associated with a reduction in the proportion of patients needing reintubation at 72 h (5% vs 12%, $p=0.004$), in the frequency of postextubation ARF (8% vs 14%, $p=0.03$), and in laryngeal oedemas requiring intubation (0% vs 3%, $p=0.001$), whereas time to reintubation was similar in both groups.⁸⁹ A meta-analysis of seven studies including the two aforementioned studies showed that HFNT significantly decreased the reintubation frequency compared with COT in 632 critically ill medical patients (RR 0.35, 95% CI 0.19–0.64; $p=0.0007$). In summary, HFNT can be an attractive and more effective approach than COT to prevent postextubation ARF in unselected ICU patients.

Several studies have assessed the effects of preventive NIV in high-risk ICU patients. Nava and co-workers⁸⁶ did the first multicentre randomised controlled trial to evaluate whether, as compared with COT and standard medical therapy, the early application of NIV immediately after extubation was effective in preventing postextubation ARF in high-risk, critically ill patients. In Nava and co-workers' study, high-risk critically ill patients were defined by the following criteria: more than one consecutive failure of the weaning trial, chronic heart failure, PaCO₂ greater than 45 mm Hg after extubation, more than one comorbidity (excluding chronic heart failure), weak cough defined as an airway care score greater than 8 and less than 12, or upper airways stridor at extubation not requiring immediate reintubation. The panel includes the most common risk factors reported in literature, including these ones (also with different terminology). The authors reported a significant reduction of reintubation frequency (4 [8%] of 48 for NIV vs 12 [24%] of 49 for COT, $p=0.03$), which in turn was associated with a lower ICU mortality, in the NIV group. In a subsequent study of 162 patients by Ferrer and colleagues, no difference in reintubation frequency was found between NIV and COT delivered through a Venturi mask in patients at risk of postextubation ARF.⁸⁴ A reduction in postextubation ARF (16% for NIV vs 33% for COT, $p=0.03$) and in ICU mortality (3% vs 14%, $p=0.015$) was statistically significant at 3 h after extubation. In addition, patients experienced less mortality and 90-day survival were similar. In patients with discomfort, fewer displacements of the interface, and fewer desaturations with HFNT. Finally, fewer patients had postextubation ARF requiring any form of ventilator support (8% for HFNT vs 35% for Venturi mask, $p<0.001$), NIV (4% vs 15%, $p=0.042$), or reintubation (4% vs 21%, $p=0.005$) in the HFNT group, suggesting a potential role of this technique in preventing extubation failure. The benefit of HFNT in reducing reintubation failure was observed mainly in patients reintubated because of hypoxaemia or inability to clear secretions.⁸⁵ Hernández and colleagues did a multicentre randomised controlled trial to assess the effects of 24 h of HFNT and COT in 527 mechanically ventilated patients (medical and surgical) at low risk for extubation (23 [15%] of 150 patients in the HFNT group vs 23 [28%] of 83 in the control group).⁸⁹ In line with the results of Maggiore and colleagues,⁸⁸ they found that use of HFNT was associated with a reduction in the proportion of patients needing reintubation at 72 h (5% vs 12%, $p=0.004$), in the frequency of postextubation ARF (8% vs 14%, $p=0.03$), and in laryngeal oedemas requiring intubation (0% vs 3%, $p=0.001$), whereas time to reintubation was similar in both groups.⁸⁹ A meta-analysis of seven studies including the two aforementioned studies showed that HFNT significantly decreased the reintubation frequency compared with COT in 632 critically ill medical patients (RR 0.35, 95% CI 0.19–0.64; $p=0.0007$). In summary, HFNT can be an attractive and more effective approach than COT to prevent postextubation ARF in unselected ICU patients.

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ventilation in critically ill adults (strong recommendation, moderate certainty of evidence).^{12,95}

Only one study compared HFNT and NIV in critically ill patients at risk of extubation failure. Hernández and co-workers did a multicentre, non-inferiority randomised controlled trial in 604 high-risk patients, comparing preventive use of HFNT or NIV, applied soon after extubation and maintained for 24 h.⁸³ HFNT was not inferior to NIV in preventing reintubation (19.1% for NIV vs 22.8% for HFNT; absolute risk difference -3.7; 95% CI -9.1 to ∞; in the multivariable analysis, the marginal odds ratio (OR) was 1.25; 95% CI 0 to 1.74), despite the postextubation ARF frequency at 72 h being higher in the NIV group (39.8% for NIV vs 26.9% for HFNT; absolute risk difference 12.9; 95% CI 6.6 to ∞), probably because of greater patient discomfort and difficulties in optimising NIV application; this possibility is also suggested by the shorter-than-planned duration of NIV in the NIV group (14 h, instead of 24 h as intended in the study protocol). As compared with NIV, HFNT is advantaged by its ease of use and the lower skill and expertise required by the operators. The results of this trial support previous findings that HFNT is very well tolerated,^{9,96} which in turn might facilitate its application and could increase patient compliance with treatment. The trial also indicated that HFNT can be an effective alternative to NIV for preventing ARF in high-risk patients, although further investigation is needed.

Postoperative setting

Because postoperative ARF increases reintubation frequency, morbidity, mortality, and length of hospital stay,^{97,98} preoperative risk scores have been developed to identify patients at risk (ie, those who are older or with obesity, COPD, or heart disease) and to apply preventive, perioperative support strategies.⁹⁹

Several studies have specifically evaluated the application of CPAP and NIV in the postoperative period for patients undergoing major surgery under a general anaesthetic. The ERS-ATS guidelines suggested NIV for patients with postoperative ARF (conditional recommendation, moderate certainty of evidence), without differentiating, however, between prophylactic or therapeutic use of NIV.¹¹ Chiumello and colleagues¹⁰⁰ did a systematic review on the use of NIV and CPAP for preventive and therapeutic purposes after various types of major surgery (abdominal, thoracic, thoraco-abdominal vascular, cardiac, and bariatric surgery). They found that, as compared with COT, either preventive NIV or CPAP in the postoperative period improved lung volumes and gas exchange and might decrease pulmonary complications, reintubations, and hospital length of stay. In a multicentre randomised controlled trial, Squadrone and colleagues assessed the effects of CPAP versus COT in 209 patients developing hypoxaemia within 1 h after abdominal surgery.¹⁰¹ The early use of CPAP, effectively as a preventive strategy, decreased frequency of reintubation

(1% vs 10%, $p=0.005$), as well as pneumonia (2% vs 10%; $p=0.02$) and sepsis (2% vs 9%; $p=0.03$).

Few trials have assessed the effects of HFNT and COT in preventing postoperative ARF in patients who have undergone cardiac or thoracic surgery.^{63,102-105} These studies reported conflicting results in terms of the effect of HFNT on atelectasis and oxygenation. One study, done in 340 patients who had undergone cardiac surgery, found that escalation in respiratory support owing to ARF onset was lower with HFNT (38% for HFNT vs 62% for COT).¹⁰² Two other studies done after thoracic surgery reported that HFNT decreased reintubations or hospital length of stay.^{103,104} These three studies, however, were not powered for these outcomes. The Bilevel Positive Airway Pressure Versus Optiflow study was the first, large, multicentre randomised controlled trial in this area, comparing HFNT and NIV in 830 patients who had undergone cardiothoracic surgery and developed hypoxaemia during the spontaneous breathing trial or after extubation.⁸⁰ In this non-inferiority trial, NIV and HFNT were applied according to three different strategies: facilitative, preventive, or curative. Treatment failure, defined as reintubation, switch to the other treatment, or premature discontinuation, was similar in both groups (21% for HFNT and 21.9% for NIV, for the three strategies combined; absolute risk difference 0.9%, 95% CI -4.9% to 6.6%, $p=0.003$), as were reintubations (14% in both groups). A post-hoc analysis showed that there were no differences in the proportion of patients with treatment failure between HFNT and NIV when these techniques were used as a facilitative strategy or as a curative strategy.⁷⁹ When considered as preventive strategies, however, treatment failure was lower in the HFNT group (6%) than in the NIV group (13%; $p=0.04$). Futier and colleagues evaluated the clinical efficacy of HFNT and COT after extubation in 220 patients at medium-to-high risk (Assess Respiratory Risk in Surgical Patients in Catalonia risk score of ≥ 26 points) of postoperative pulmonary complications after major abdominal surgery (OPERA trial).¹⁰⁶ No difference was found between the two groups in the proportion of patients with hypoxaemia ($\text{PaO}_2/\text{FiO}_2 \leq 300$) at 1 h after extubation and at treatment discontinuation. Postoperative pulmonary complications, duration of hospital stay, and hospital mortality were also similar between groups. Given the paucity of data available in patients undergoing major abdominal surgery and the results of the OPERA trial, the potential usefulness of HFNT after extubation in these patients remains unclear.

Therapeutic strategy

Therapeutic strategies of ventilatory support are applied in cases of postextubation ARF, with the aim of avoiding reintubation both in critically ill medical patients and in the postoperative setting.

Critically ill medical patients

The ERS-ATS guidelines suggested that NIV should not be used in the treatment of medical patients with

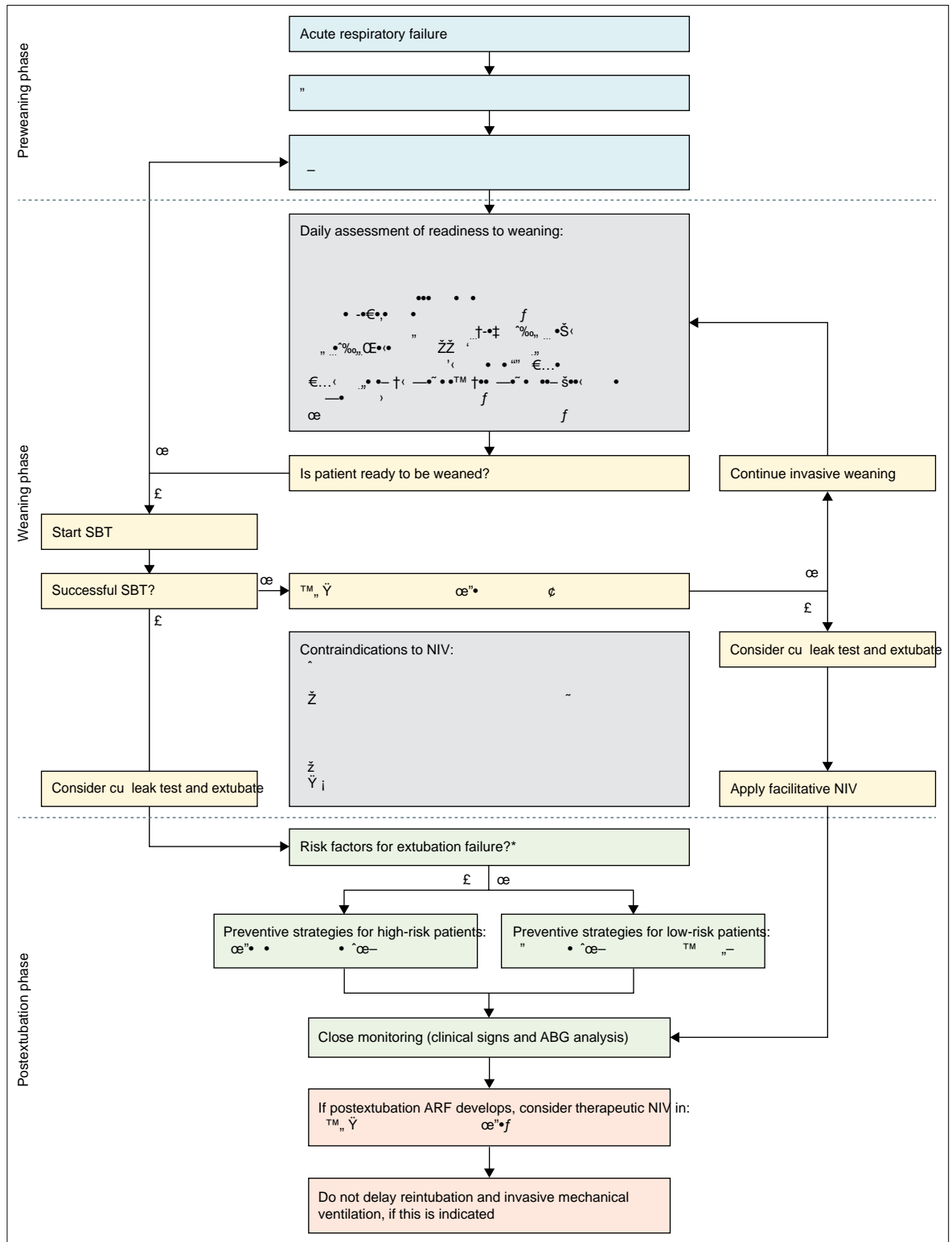


Figure : Algorithm for ventilatory support after extubation in critically ill medical patients
 HR=heart rate. BP=blood pressure. SpO₂=pulse-oximeter oxygen saturation. F_IO₂=fraction of inspired oxygen. PaO₂=arterial partial pressure of oxygen. RR=respiratory rate. MIP=maximal inspiratory pressure. VT=tidal volume. VC=vital capacity. SBT=spontaneous breathing trial. COPD=chronic obstructive pulmonary disease. NIV=non-invasive ventilation. HFNT=high-flow nasal therapy. COT=conventional oxygen therapy. ABG=arterial blood gas. ARF=acute respiratory failure. * See panel.

established postextubation ARF (conditional recommendation, low certainty of evidence). This suggestion was based on the results of two randomised controlled trials comparing the effects of NIV and COT on clinical outcome.^{8,107} In a single-centre randomised controlled trial, Keenan and colleagues⁸ randomly assigned 81 high-risk patients with postextubation respiratory distress to NIV or COT and found no difference in the proportion needing reintubation (72% vs 69%; RR 1.04, 95% CI 0.78–1.38) or hospital mortality (31% for both groups RR 0.99, 95% CI 0.52–1.91).⁹⁷ Esteban and colleagues did a multicentre randomised controlled trial to evaluate the effect of NIV versus COT on all-cause mortality in 221 patients with postextubation ARF. No differences were found in reintubation frequency and ICU length of stay. In the NIV group, however, ICU all-cause mortality was higher (25% vs 14%; RR 1.78, 95% CI 1.03–3.20, $p=0.048$) and the time between onset of respiratory distress and reintubation was longer in the NIV group (median, 12 h, IQR, 2 h 10 min–28 h) than in the standard-therapy group (median, 2 h 30 min, IQR, 45 min–16 h 30 min, $p=0.02$; RR and CI not indicated for this outcome), suggesting that delay in reintubation might worsen outcomes. Of note, these two trials enrolled few patients with COPD who had postextubation ARF, and therefore their results cannot apply to this condition.

To our knowledge, no data on the therapeutic use of HFNT in critically ill medical patients is available to date.

Postoperative setting

By contrast with medical patients, the ERS–ATS guidelines suggested NIV for patients with postoperative ARF (conditional recommendation, moderate certainty of evidence) for therapeutic purposes.⁸ Chiumello and colleagues reported that, as compared with COT, therapeutic NIV and CPAP in the postoperative period improved atelectasis and gas exchange and might decrease reintubations, mortality, ICU length of stay, and complications.¹⁰⁰ In particular, studies have shown that therapeutic NIV can improve outcomes after thoracic and abdominal surgery and in patients undergoing solid organ transplantation.^{101,108–111} Auriant and colleagues⁹⁹ reported that, as compared with COT, NIV could reduce the need for reintubation (21% vs 50%; $p=0.035$) and hospital mortality (13% vs 38%; $p=0.045$) in 48 patients developing ARF after lung resection. Jaber and colleagues¹⁰² did a multicentre randomised controlled trial comparing NIV and COT in 293 patients developing postoperative ARF following abdominal surgery. NIV decreased the proportion of patients with reintubation occurring within 7 days (33% vs 46%; $p=0.03$) and healthcare-associated infections (31% vs 49%; $p=0.003$). In 40 patients with postoperative ARF after solid organ transplantation, Antonelli and colleagues found that NIV, as compared with COT, improved oxygenation and decreased the need for reintubation (20% vs 70%; $p=0.002$), frequency of complications, and ICU mortality.¹⁰⁸

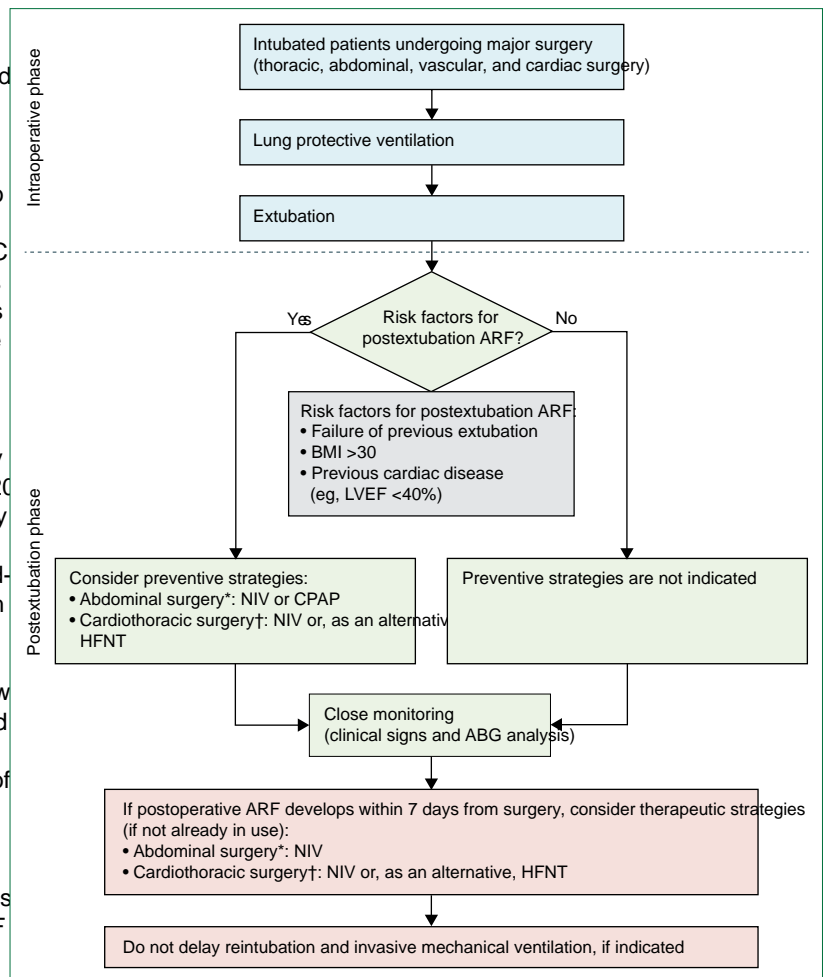


Figure 1: Algorithm for ventilatory support after extubation in postoperative setting. ARF=acute respiratory failure. BMI=body mass index. LVEF=left ventricular ejection fraction. NIV=non-invasive ventilation. CPAP=continuous positive airway pressure. HFNT=high-flow nasal therapy. ABG=arterial blood gas. *Abdominal surgery includes abdominal vascular surgery. †Cardiothoracic surgery includes thoracic vascular surgery.

In patients developing ARF after cardiothoracic surgery, HFNT and NIV are equally effective in avoiding abdominal surgery and in patients undergoing solid organ transplantation.^{101,108–111} A post-hoc analysis of the Bilevel Positive Airway Pressure Versus Opti-Flow non-inferiority trial¹⁰³ showed, in fact, that there were no differences in treatment failure between the two techniques, when used in the context of a therapeutic strategy (27% for HFNT vs 28% for NIV, $p=0.93$). This might suggest that postoperative HFNT can be used as a first-line, non-invasive technique of respiratory support after cardiothoracic surgery because it is non-inferior to NIV overall, could even decrease the need for reintubation occurring within 7 days (33% vs 46%; $p=0.03$) and healthcare-associated infections (31% vs 49%; $p=0.003$). In 40 patients with postoperative ARF after solid organ transplantation, Antonelli and colleagues found that NIV, as compared with COT, improved oxygenation and decreased the need for reintubation (20% vs 70%; $p=0.002$), frequency of complications, and ICU mortality.¹⁰⁸

Clinical implications

Weaning from mechanical ventilation is a complex process that should start as early as possible,

theoretically soon after the beginning of mechanical exacerbation or heart failure compared to non-ventilation, and continues up to the time when a hypercapnic patients, non-COPD patients, and patients possible postextubation ARF occurs and must be without heart failure,^{84,93} whereas the use of NIV is managed (figure 2). The first step is, therefore, debated in patients with hypoxaemic ARF. Preventive represented by an appropriate management of invasive NIV should be started immediately after extubation and mechanical ventilation based on lung protection. This applied continuously for at least the first 24 h. In high-prerequisite is valid both for critically ill medical risk patients, HFNT can be used as an alternative to NIV, patients and for patients undergoing a surgical because it is not inferior to NIV in preventing postextubation procedure, in which potential lung injury due to non-intubation ARF and is associated with better patient comfort protective, intraoperative mechanical ventilation is and greater ease of use. Besides the availability of often underestimated.¹² Lung injury can result in a devices, the choice of NIV or HFNT in these patients longer invasive ventilation and in a higher risk of depends on personnel skill and expertise with these difficult weaning and postextubation ARF compared techniques (figure 3).⁸³ If postextubation ARF develops, with patients without lung injury.¹¹² NIV is not recommended as a curative strategy in

After extubation, available strategies of respiratory medical patients and intubation should be preferred. support should be chosen based on the type of patient. In selected patients with COPD, however, a trial of NIV (medical or surgical), the level of risk of postextubation could be considered, if applied in a safe environment ARF, and the cause of ARF (table 1, figures 3 and 4) (figure 3).¹¹

Table 2 lists suggested settings for different techniques. In the postoperative setting, preventive strategies of ventilatory support after extubation. should be considered in case of a high risk of

Critically ill medical patients should undergo a daily postextubation ARF. Different options exist according to assessment of their ability to breathe unassisted to the type of surgery. After abdominal and abdominal evaluate as early as possible the possibility of extubation. vascular surgery, early NIV or CPAP are beneficial.¹¹¹

At this stage, it is also important to assess whether the. After cardiothoracic surgery, including thoracic vascular patient has risk factors for extubation failure (panel). In surgery, NIV is also useful. In these patients, HFNT can selected categories of patients, such as those with COPD. be used as an alternative to NIV; it has similar effects on or developing hypercapnia during the spontaneous outcome and can be easier to use (figure 4).⁹² If

breathing trial, early extubation and facilitative NIV postextubation ARF develops within 7 days from surgery, should be considered even after failure of the provided that surgical complications are excluded and spontaneous breathing trial, if some degree of recovery the patient is cooperative and able to protect their air from the initial cause of ARF has been achieved (ie, afterward, NIV should be considered in patients who have 48 h) and no contraindication to NIV exists (figure 3).^{71,72,74} undergone abdominal or cardiothoracic surgery.^{11,109,111} In

After a successful spontaneous breathing trial, strategies cardiothoracic surgery, HFNT can be used as an different according to risk of extubation failure. If no risk alternative to NIV (figure 4).^{11,80}

factor has been identified (low-risk patients), HFNT is. In any case, in both medical and surgical patients, the the preferable preventive strategy if the device is use of any technique of postextubation respiratory support available, given the advantages over COT (figure 3).^{93,92} should not delay intubation and escalation to invasive

In high-risk patients, NIV might prevent postextubation mechanical ventilation when this is more appropriate, ARF compared with COT.¹ This protective effect is because delay can worsen the patient's outcome and greater in hypercapnic patients and those with COPD increase mortality (figures 3 and 4).^{8,113,114}

	NIV	CPAP	HFNT
Settings	Ventilatory mode: pressure support ventilation; PSV level: 5–15 cm H ₂ O; PEEP: 4–5 cm H ₂ O, up to 8–10 cm H ₂ O; Inspiratory trigger sensitivity: as high as possible while avoiding autotriggering (eg, flow trigger 1–2 L/min); pressurisation ramp: high (eg, 80% on a scale 0–100%); expiratory trigger: 25–30% (up to 50–60% in patients with any chronic obstructive pathology with increased time constant and dynamic hyperinflation); lowest to reach the SpO ₂ target	PEEP: 5–10 cm H ₂ O; Total gas flow: 30–40 L/min, according to patient comfort; gas rebreathing; F _{IO} : the lowest to reach the SpO ₂ target	Gas flow: 30–60 L/min, according to patient comfort and gas flow (higher temperature with higher gas flow); F _{IO} : the lowest to reach the SpO ₂ target
Targets	Tidal volume: 6–8 mL/kg predicted body weight; respiratory rate 30 breaths/min; SpO ₂ : 92–98% or 88–92% in patients with chronic respiratory disease	Respiratory rate 30 breaths/min; SpO ₂ : 92–98% or 88–92% in patients with chronic respiratory disease	Respiratory rate 30 breaths/min; SpO ₂ : 92–98% or 88–92% in patients with chronic respiratory disease
NIV=non-invasive ventilation. CPAP=continuous positive airway pressure. HFNT=high-flow nasal therapy. PSV=pressure support ventilation. PEEP=positive end-expiratory pressure. F _{IO} =inspired oxygen fraction. SpO ₂ =pulse-oximeter oxygen saturation.			
Table 2: Suggested starting settings for NIV, CPAP, and HFNT after extubation			

Study title (abbreviation)	Design	Intervention	Primary outcome
NCT02107183 Impact of nasal high- ow vs Venturi mask oxygen therapy on weaning outcome: a multicenter, randomized, controlled trial (RINO)	Interventional, phase not applicable; projected n=500	Opti ow (Fisher & Paykel Healthcare) vs Venturi mask	Reintubation within 72 h after extubation or at ICU discharge
NCT03246893 E cacy of HFNCs NIV for preventing reintubation in sepsis patients	Interventional, phase not applicable; projected n=210	Non-invasive positive pressure ventilation vs high- ow oxygen nasal cannula	Device failure rate
NCT03361683 Postextubation high- ow nasal oxygen for preventing extubation failure	Interventional, phase not applicable; projected n=170	High- ow nasal oxygen vs Venturi mask	Postextubation failure
NCT03495947 HFNC in immediately post extubation	Observational; projected n=150	HFNC	Extubation failure
NCT02290548 E ect of high- ow nasal oxygen on extubation outcome	Interventional, phase not applicable; projected n=400	HFNC immediately used after extubation vs standard oxygen therapy	Reintubation rate
NCT03441854 HFNC vs conventional oxygen therapy after extubation in liver transplantation	Observational; projected n=30	HFNC oxygen delivery after extubation vs Venturi mask	Post-operative oxygenation measured at 1 h after extubation
NCT01928238 Physiological e ects of non-invasive neurally adjusted ventilatory assist (NAVA) vs noninvasive pressure support ventilation in patients at risk for respiratory distress needed preventive use of non-invasive ventilation after extubation (NIV-NAVA)	Interventional, phase not applicable; projected n=13	Non-invasive neurally adjusted ventilatory assist (NIV-NAVA) vs non-invasive pressure support ventilation (NPSV)	Respiratory muscle e ort
NCT03288311 Protocolised postextubation respiratory support study (PROPER)	Interventional, phase not applicable; projected n=630	Protocolised postextubation respiratory support vs usual care	Rate of reintubation within the 96 h after extubation
NCT03562000 Preventing extubation failure related to cough (PREXFAIL)	Interventional, phase 3; projected n=368	Cough assistance and systematic non-invasive ventilation	Reintubation rate, including every cause
NCT01967108 Postextubation chest physiotherapy in ICU	Interventional, phase not applicable; projected n=65	Chest physiotherapy	Rate of reintubation within the 48 h after extubation

HFNC=high- ow nasal cannula. ICU=intensive care unit.

Table : Ongoing studies on respiratory support after extubation (from ClinicalTrials.gov)

Areas of uncertainty and future research

There are several areas of uncertainty concerning the use of ventilatory support after extubation. How to individually tailor treatment to protect extubation is not clear, a relevant issue in the era of precision medicine and personalisation of care. The variability in inclusion and exclusion criteria creates considerable heterogeneity among published studies. We need, therefore, to better characterise patients at risk of extubation failure, which implies a better definition of risk factors for postextubation ARF. Understanding the mechanistic linkage between causes and symptoms of postextubation ARF would allow improved selection of treatments for individual patients. Data suggest that the choice of interface, such as helmets versus masks, could affect outcome of NIV.¹¹⁵ Assessing the role of different NIV interfaces and emerging technologies such as HFNT or extracorporeal gas exchange will certainly be areas of future research. Treatment dose, timing, and intensity (therapeutic) is not fully elucidated, especially for both established practices (NIV, CPAP) and new specific categories of patients such as those without hypercapnia, and will need further investigation, as will be needed. The value of different postextubation other technologies such as electrical pacing of the

Search strategy and selection criteria

We used our existing knowledge of publications on the subject and identified additional references for this Review through searches of PubMed for articles published from Jan 1, 1970, to April 30, 2018, using the search terms “noninvasive ventilation”, “continuous positive airway pressure”, “high- ow nasal cannula”, “nasal high- ow”, “nasal high- ow oxygen”, “oxygen therapy”, “extubation”, “weaning”, and “acute respiratory failure”, with different combinations. The search was limited to studies done in adult humans (> 18 years old). We reviewed articles resulting from these searches and references cited in those articles and we selected the relevant ones. We included articles published in English, French, Italian, Spanish, and German.

diaphragm by transvenous phrenic nerve stimulation to reduce diaphragm dysfunction.¹¹⁶ Finally, early physiotherapy could play an important part in the weaning process.¹⁷ Research in these areas is ongoing and could contribute to improvement of weaning outcome (table 3).

Conclusions

Non-invasive ventilatory support after extubation has an important role in improving the outcome of weaning from invasive mechanical ventilation. Several techniques are available nowadays and others are emerging. These techniques are incorporated in different strategies to facilitate extubation, and to prevent or to treat post-extubation ARF. Guidelines should direct the implementation of NIV strategies in everyday clinical practice. In some areas, research is ongoing and additional evidence is needed. For instance, it will be important to precisely define the risk factors for extubation failure, the relative value of NIV and HFNT, and the dose, timing, and duration of postextubation respiratory support to help clinicians to use the right device, with the right setting, in the right patient, at the right time.

Contributors

SMM conceived the idea for this Review. MB and SMM contributed to the literature search and developed the first draft. LS, MB and SMM prepared the figures. SMM and FP revised and finalised the manuscript and the figures. All authors contributed to and approved the final version of the report.

Declaration of interests

We declare no competing interests.

References

- Boles JM, Bion J, Connors A, et al. Weaning from mechanical ventilation. *Eur Respir J* 2007; 29: 1033–56.
- Esteban A, Frutos-Vivar F, Muriel A, et al. Evolution of mortality over time in patients receiving mechanical ventilation. *Am J Respir Crit Care Med* 2013; 188: 220–30.
- Thille AW, Richard JC, Brochard L. The decision to extubate in the intensive care unit. *Am J Respir Crit Care Med* 2013; 187: 1294–302.
- Epstein SK, Ciubotaru RL, Wong JB. Effect of failed extubation on the outcome of mechanical ventilation. *Chest* 1997; 112: 186–92.
- Esteban A, Alia I, Gordo F, et al. Extubation outcome after spontaneous breathing trials with tube or pressure support ventilation. The Spanish Lung Failure Collaborative Group. *Am J Respir Crit Care Med* 1997; 156 (2 pt 1): 459–65.
- Frutos-Vivar F, Esteban A, Pezterguia C, et al. Outcome of reintubated patients after scheduled extubation. *J Crit Care* 2011; 26: 502–09.
- Thille AW, Harrois A, Schortgen F, Brun-Buisson C, Brochard L. Outcomes of extubation failure in medical intensive care unit patients. *Crit Care Med* 2011; 39: 2612–18.
- Esteban A, Frutos-Vivar F, Ferguson ND, et al. Noninvasive positive-pressure ventilation for respiratory failure after extubation. *N Engl J Med* 2004; 350: 2452–60.
- Maggiore SM, Idone FA, Vaschetto R, et al. High-flow versus Venturi mask oxygen therapy after extubation. Effects on oxygenation, comfort, and clinical outcome. *Am J Respir Crit Care Med* 2014; 190: 282–88.
- Papazian L, Corley A, Hsiao D, et al. Use of high-flow nasal cannula oxygenation in ICU adults: a narrative review. *Intensive Care Med* 2016; 42: 1336–49.
- Rochwerf B, Brochard L, Elliott MW, et al. Official ERAS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. *Eur Respir J* 2017; 50: 1602426.

- Schmidt GA, Girard TD, Kress JP, et al. Official Executive Summary of an American Thoracic Society/American College of Chest Physicians Clinical Practice Guideline: liberation from mechanical ventilation in critically ill adults. *Am J Respir Crit Care Med* 2017; 195: 115–19.
- Jaber S, Chanques G, Matecki S, et al. Post-extubation stridor in intensive care unit patients. Risk factors evaluation and importance of the cu-leak test. *Intensive Care Med* 2003; 29: 69–74.
- Pluijms WA, van Mook WN, Wittekamp BH, Bergmans DC. Postextubation laryngeal edema and stridor resulting in respiratory failure in critically ill adult patients: updated review. *Crit Care* 2015; 19: 295.
- Straus C, Louis B, Isabey D, Lemaire F, Harf A, Brochard L. Contribution of the endotracheal tube and the upper airway to breathing workload. *Am J Respir Crit Care Med* 1998; 157: 23–30.
- Girard TD, Alhazzani W, Kress JP, et al. An Official American Thoracic Society/American College of Chest Physicians Clinical Practice Guideline: liberation from mechanical ventilation in critically ill adults. Rehabilitation protocols, ventilator liberation protocols, and cu-leak tests. *Am J Respir Crit Care Med* 2017; 195: 120–33.
- Wittekamp BH, van Mook WN, Tan DH, Zwaveling JH, Bergmans DC. Clinical review: post-extubation laryngeal edema and extubation failure in critically ill adult patients. *Crit Care* 2009; 13: 233.
- Mauri T, Grasselli G, Jaber S. Respiratory support after extubation: noninvasive ventilation or high-flow nasal cannula, as appropriate. *Ann Intensive Care* 2017; 7: 52.
- Soummer A, Perbet S, Brisson H, et al. Ultrasound assessment of lung aeration loss during a successful weaning trial predicts postextubation distress. *Crit Care Med* 2012; 40: 2064–72.
- Mekontso-Dessap A, de Prost N, Girou E, et al. B-type natriuretic peptide and weaning from mechanical ventilation. *Intensive Care Med* 2006; 32: 1529–36.
- Navalesi P, Maggiore SM. Positive End-Expiratory Pressure. In: Tobin MJ, ed. Principles and practice of mechanical ventilation, 3rd edn. New York: McGraw-Hill, 2012: 253–302.
- Hamaya Y, Dohi S. Differences in cardiovascular response to airway stimulation at different sites and blockade of the responses by lidocaine. *Anesthesiology* 2000; 93: 95–103.
- Sharma VB, Prabhakar H, Rath GP, Bithal PK. Comparison of dexmedetomidine and lignocaine on attenuation of airway and pressor responses during tracheal extubation. *J Neuroanaesthesiol Crit Care* 2014; 1: 50–55.
- Jaber S, Petrof BJ, Judg B, et al. Rapidly progressive diaphragmatic weakness and injury during mechanical ventilation in humans. *Am J Respir Crit Care Med* 2011; 183: 364–71.
- Goligher EC, Dres M, Fan E, et al. Mechanical ventilation-induced diaphragm atrophy strongly impacts clinical outcomes. *Am J Respir Crit Care Med* 2018; 197: 204–13.
- Penuelas O, Muriel A, Frutos-Vivar F, et al. Prediction and outcome of intensive care unit-acquired paresis. *J Intensive Care Med* 2018; 33: 16–28.
- Dres M, Dube BP, Mayaux J, et al. Coexistence and impact of limb muscle and diaphragm weakness at time of liberation from mechanical ventilation in medical intensive care unit patients. *Am J Respir Crit Care Med* 2017; 195: 57–66.
- Dube BP, Dres M, Mayaux J, Demiri S, Similowski, Demoule A. Ultrasound evaluation of diaphragm function in mechanically ventilated patients: comparison to phrenic stimulation and prognostic implications. *Thorax* 2017; 72: 811–18.
- Jung B, Moury PH, Mahul M, et al. Diaphragmatic dysfunction in patients with ICU-acquired weakness and its impact on extubation failure. *Intensive Care Med* 2016; 42: 853–61.
- The American Thoracic Society, the European Respiratory Society, the European Society of Intensive Care Medicine, the Societe de Reanimation de Langue Francaise. International Consensus Conferences in Intensive Care Medicine: noninvasive positive pressure ventilation in acute respiratory failure. *Am J Respir Crit Care Med* 2001; 163: 283–91.
- Demoule A, Girou E, Richard JC, Taille S, Brochard L. Increased use of noninvasive ventilation in French intensive care units. *Intensive Care Med* 2006; 32: 1747–55.
- Vitacca M, Ambrosino N, Cini E, et al. Physiological response to pressure support ventilation delivered before and after extubation in patients not capable of totally spontaneous autonomous breathing. *Am J Respir Crit Care Med* 2001; 164: 638–41.

- 33 Girou E, Brun-Buisson C, Taille S, Lemaire F, Brochard L. Secular trends in nosocomial infections and mortality associated with noninvasive ventilation in patients with exacerbation of COPD and pulmonary edema. *JAMA* 2003; **290**: 2985–91.
- 34 Jiang JS, Kao SJ, Wang SN. Effect of early application of biphasic positive airway pressure on the outcome of extubation in ventilator weaning. *Respirology* 1999; **4**: 161–65.
- 35 Jaber S, Michelet P, Chanques G. Role of non-invasive ventilation (NIV) in the perioperative period. *Best Pract Res Clin Anaesthesiol* 2010; **24**: 253–65.
- 36 L'Her E, Deye N, Lellouche F, et al. Physiologic effects of noninvasive ventilation during acute lung injury. *Am J Respir Crit Care Med* 2005; **172**: 1112–18.
- 37 Brochard L, Isabey D, Piquet J, et al. Reversal of acute exacerbations of chronic obstructive lung disease by inspiratory assistance with a face mask. *N Engl J Med* 1990; **323**: 1523–30.
- 38 Nava S, Bruschi C, Rubini F, Palo A, Iotti G, Braschi A. Respiratory response and inspiratory effort during pressure support ventilation in COPD patients. *Intensive Care Med* 1995; **21**: 871–79.
- 39 Ranieri VM, Dambrosio M, Brienza N. Intrinsic PEEP and cardiopulmonary interaction in patients with COPD and acute ventilatory failure. *Eur Respir J* 1996; **9**: 1283–92.
- 40 Katz JA, Marks JD. Inspiratory work with and without continuous positive airway pressure in patients with acute respiratory failure. *Anesthesiology* 1985; **63**: 598–607.
- 41 Lenique F, Habis M, Lofaso F, Dubois-Randé JL, Harf A, Brochard L. Ventilatory and hemodynamic effects of continuous positive airway pressure in left heart failure. *Am J Respir Crit Care Med* 1997; **155**: 500–05.
- 42 Marini JJ, Culver BH, Butler J. Mechanical effect of lung distention with positive pressure on cardiac function. *Am Rev Respir Dis* 1981; **124**: 382–86.
- 43 Jardin F, Farcot JC, Boisante L, Curien N, Margairaz A, Bourdarias JP. Influence of positive end-expiratory pressure on left ventricular performance. *N Engl J Med* 1981; **304**: 387–92.
- 44 Naughton MT, Rahman MA, Hara K, Floras JS, Bradley TD. Effect of continuous positive airway pressure on intrathoracic and left ventricular transmural pressures in patients with congestive heart failure. *Circulation* 1995; **91**: 1725–31.
- 45 Rasanen J, Heikkilä J, Downs J, Nikki P, Vaisanen I, Viitanen A. Continuous positive airway pressure by face mask in acute cardiogenic pulmonary edema. *Am J Cardiol* 1985; **55**: 296–300.
- 46 Bersten AD, Holt AW, Vedig AE, Skowronski GA, Baggoley CJ. Treatment of severe cardiogenic pulmonary edema with continuous positive airway pressure delivered by face mask. *N Engl J Med* 1991; **325**: 1825–30.
- 47 Masip J, Betbese AJ, Paez J, et al. Non-invasive pressure support ventilation versus conventional oxygen therapy in acute cardiogenic pulmonary oedema: a randomised trial. *Lancet* 2000; **356**: 2126–32.
- 48 Lee JH, Rehder KJ, Williford L, Cheifetz IM, Turner DA. Use of high flow nasal cannula in critically ill infants, children, and adults: a critical review of the literature. *Intensive Care Med* 2013; **39**: 247–57.
- 49 Parke RL, Bloch A, McGuinness SP. Effect of very-high-flow nasal therapy on airway pressure and end-expiratory lung impedance in healthy volunteers. *Respir Care* 2015; **60**: 1397–403.
- 50 Dysart K, Miller TL, Wolfson MR, Shaffer TH. Research in high flow therapy: mechanisms of action. *Respir Med* 2009; **103**: 1400–05.
- 51 Goligher EC, Slutsky AS. Not just oxygen? Mechanisms of benefit from high-flow nasal cannula in hypoxic respiratory failure. *Am J Respir Crit Care Med* 2017; **195**: 1128–31.
- 52 Spoletini G, Alotaibi M, Blasi F, Hill NS. Heated humidified high-flow nasal oxygen in adults: mechanisms of action and clinical implications. *Chest* 2015; **148**: 253–61.
- 53 Groves N, Tobin A. High flow nasal oxygen generates positive airway pressure in adult volunteers. *Aust Crit Care* 2007; **20**: 126–31.
- 54 Mundel T, Feng S, Tatkov S, Schneider H. Mechanisms of nasal high flow on ventilation during wakefulness and sleep. *J Appl Physiol* 2013; **114**: 1058–65.
- 55 Mauri T, Turrini C, Eronia N, et al. Physiologic effects of high-flow nasal cannula in acute hypoxic respiratory failure. *Am J Respir Crit Care Med* 2017; **195**: 1207–15.
- 56 Chanques G, Riboulet F, Molinari N, et al. Comparison of three high flow oxygen therapy delivery devices: a clinical physiological cross-over study. *Minerva Anestesiol* 2013; **79**: 1344–55.
- 57 Roca O, Riera J, Torres F, Masclans JR. High-flow oxygen therapy in acute respiratory failure. *Respir Care* 2010; **55**: 408–13.
- 58 Wettstein RB, Shelledy DC, Peters JI. Delivered oxygen concentrations using low-flow and high-flow nasal cannulas. *Respir Care* 2005; **50**: 604–09.
- 59 Ritchie JE, Williams AB, Gerard C, Hockey H. Evaluation of a humidified nasal high-flow oxygen system, using oxygraphy, capnography and measurement of upper airway pressures. *Anaesth Intensive Care* 2011; **39**: 1103–10.
- 60 Moller W, Feng S, Domanski U, et al. Nasal high flow reduces dead space. *J Appl Physiol* 2017; **122**: 191–97.
- 61 Moller W, Celik G, Feng S, et al. Nasal high flow clears anatomical dead space in upper airway models. *J App Physiol* 2015; **118**: 1525–32.
- 62 Parke RL, Eccleston ML, McGuinness SP. The effects of flow on airway pressure during nasal high-flow oxygen therapy. *Respir Care* 2011; **56**: 1151–55.
- 63 Corley A, Caruana LR, Barnett AG, Tronstad O, Fraser JF. Oxygen delivery through high-flow nasal cannulae increase end-expiratory lung volume and reduce respiratory rate in post-cardiac surgical patients. *Br J Anaesth* 2011; **107**: 998–1004.
- 64 Hasani A, Chapman TH, McCool D, Smith RE, Dilworth JP, Agnew JE. Domiciliary humidification improves lung mucociliary clearance in patients with bronchiectasis. *Chron Respir Dis* 2008; **5**: 81–86.
- 65 Costello RW, Liston R, McNicholas WT. Compliance at night with low flow oxygen therapy: a comparison of nasal cannulae and Venturi face masks. *Thorax* 1995; **50**: 405–06.
- 66 McGinley BM, Patil SP, Kirkness JP, Smith PL, Schwartz AR, Schneider H. A nasal cannula can be used to treat obstructive sleep apnea. *Am J Respir Crit Care Med* 2007; **176**: 194–200.
- 67 O'Driscoll BR, Howard LS, Davison AG. BTS guideline for emergency oxygen use in adult patients. *Thorax* 2008; **63** (suppl 6): 1–68.
- 68 Kallstrom TJ. AARC clinical practice guideline: oxygen therapy for adults in the acute care facility—2002 revision & update. *Respir Care* 2002; **47**: 717–20.
- 69 Jones HA, Turner SL, Hughes JM. Performance of the large-reservoir oxygen mask (Ventimask). *Lancet* 1984; **1**: 1427–31.
- 70 Antonelli M, Bello G. Noninvasive mechanical ventilation during the weaning process: facilitative, curative, or preventive? *Crit Care* 2008; **12**: 136.
- 71 Esteban A, Anzueto A, Frutos F, et al. Characteristics and outcomes in adult patients receiving mechanical ventilation: a 28-day international study. *JAMA* 2002; **287**: 345–55.
- 72 Nava S, Ambrosino N, Clini E, et al. Noninvasive mechanical ventilation in the weaning of patients with respiratory failure due to chronic obstructive pulmonary disease. A randomized, controlled trial. *Ann Intern Med* 1998; **128**: 721–8.
- 73 Girault C, Daudenthun I, Chevron V, Tamion F, Leroy J, Bonmarchand G. Noninvasive ventilation as a systematic extubation and weaning technique in acute-on-chronic respiratory failure: a prospective, randomized controlled study. *Am J Respir Crit Care Med* 1999; **160**: 86–92.
- 74 Girault C, Bubenheim M, Abroug F, et al. Noninvasive ventilation and weaning in patients with chronic hypercapnic respiratory failure: a randomized multicenter trial. *Am J Respir Crit Care Med* 2011; **184**: 672–79.
- 75 Ferrer M, Esquinas A, Arancibia F, et al. Noninvasive ventilation during persistent weaning failure: a randomized controlled trial. *Am J Respir Crit Care Med* 2003; **168**: 70–76.
- 76 Burns KE, Meade MO, Premji A, Adhikari NK. Noninvasive positive-pressure ventilation as a weaning strategy for intubated adults with respiratory failure. *Cochrane Database Syst Rev* 2013; **12**: CD004127.
- 77 Burns KE, Meade MO, Premji A, Adhikari NK. Noninvasive ventilation as a weaning strategy for mechanical ventilation in adults with respiratory failure: a Cochrane systematic review. *CMAJ* 2014; **186**: E112–E22.

- 78 Vaschetto R, Turucz E, Dellapiazza F, et al. Noninvasive ventilation after early extubation in patients recovering from hypoxemic acute respiratory failure: a single-centre feasibility study. *Intensive Care Med* 2012; **38**: 1599–606.
- 79 Stephan F. High-flow nasal oxygen therapy for postextubation acute hypoxemic respiratory failure—reply. *JAMA* 2015; **314**: 1644–45.
- 80 Stephan F, Barrucand B, Petit P, et al. High-flow nasal oxygen vs noninvasive positive airway pressure in hypoxemic patients after cardiothoracic surgery: a randomized clinical trial. *JAMA* 2015; **313**: 2331–39.
- 81 Frutos-Vivar F, Ferguson ND, Esteban A, et al. Risk factors for extubation failure in patients following a successful spontaneous breathing trial. *Chest* 2006; **130**: 1664–71.
- 82 Vallverdu I, Calaf N, Subirana M, Net A, Benito S, Mancebo J. Clinical characteristics, respiratory functional parameters, and outcome of a two-hour T-piece trial in patients weaning from mechanical ventilation. *Am J Respir Crit Care Med* 1998; **158**: 1855–62.
- 83 Hernández G, Vaquero C, Colinas L, et al. Effect of postextubation high-flow nasal cannula vs noninvasive ventilation on reintubation and postextubation respiratory failure in high-risk patients: a randomized clinical trial. *JAMA* 2016; **316**: 1565–74.
- 84 Ferrer M, Valencia M, Nicolas JM, Bernadich O, Badia JR, Torres A. Early noninvasive ventilation averts extubation failure in patients at risk: a randomized trial. *Am J Respir Crit Care Med* 2006; **173**: 164–70.
- 85 Nava S, Gregoretti C, Fanfulla F, et al. Noninvasive ventilation to prevent respiratory failure after extubation in high-risk patients. *Crit Care Med* 2005; **33**: 2465–70.
- 86 Smina M, Salam A, Khamiees M, Gada P, Amoateng-Adjepong Y, Manthous CA. Cough peak flows and extubation outcomes. *Chest* 2003; **124**: 262–68.
- 87 Capdevila XJ, Perrigault PF, Perey PJ, Roustan JP, d'Athis F. Occlusion pressure and its ratio to maximum inspiratory pressure are useful predictors for successful extubation following T-piece weaning trial. *Chest* 1995; **108**: 482–89.
- 88 Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. *New Eng J Med* 1991; **324**: 1445–50.
- 89 Hernández G, Vaquero C, Gonzalez P, et al. Effect of postextubation high-flow nasal cannula vs conventional oxygen therapy on reintubation in low-risk patients: a randomized clinical trial. *JAMA* 2016; **315**: 1354–61.
- 90 Hess DR. The role of noninvasive ventilation in the ventilator discontinuation process. *Respir Care* 2012; **57**: 1619–25.
- 91 Su CL, Chiang LL, Yang SH, et al. Preventive use of noninvasive ventilation after extubation: a prospective, multicenter randomized controlled trial. *Respir Care* 2012; **57**: 204–10.
- 92 Huang HW, Sun XM, Shi ZH, et al. Effect of high-flow nasal cannula oxygen therapy versus conventional oxygen therapy and noninvasive ventilation on reintubation rate in adult patients after extubation: a systematic review and meta-analysis of randomized controlled trials. *J Intensive Care Med* 2017; published online April 21. DOI:10.1177/885066617705118.
- 93 Ferrer M, Sellares J, Valencia M, et al. Non-invasive ventilation after extubation in hypercapnic patients with chronic respiratory disorders: randomised controlled trial. *Lancet* 2009; **374**: 1082–88.
- 94 Thille AW, Boissier F, Ben-Ghezala H, et al. Easily identified at-risk patients for extubation failure may benefit from noninvasive ventilation: a prospective before-after study. *Crit Care* 2016; **20**: 48.
- 95 Ouellette DR, Patel S, Girard TD, et al. Liberation from mechanical ventilation in critically ill adults: an Official American College of Chest Physicians/American Thoracic Society Clinical Practice Guideline: inspiratory pressure augmentation during spontaneous breathing trials, protocols minimizing sedation, and noninvasive ventilation immediately after extubation. *Chest* 2017; **151**: 166–80.
- 96 Cuquemelle E, Pham T, Papon JF. Heated and humidified high-flow oxygen therapy reduces discomfort during hypoxemic respiratory failure. *Respir Care* 2012; **57**: 1571–77.
- 97 Khuri SF, Henderson WG, DePalma RG, et al. Determinants of long-term survival after major surgery and the adverse effect of postoperative complications. *Ann Surg* 2005; **242**: 326–41; discussion 41–3.
- 98 Shander A, Fleisher LA, Barie PS, Bigatello LM, Sladen RN, Watson CB. Clinical and economic burden of postoperative pulmonary complications: patient safety summit on definition, risk-reducing interventions, and preventive strategies. *Crit Care Med* 2011; **39**: 2163–72.
- 99 Canet J, Gallart L, Gomar C, et al. Prediction of postoperative pulmonary complications in a population-based surgical cohort. *Anesthesiology* 2010; **113**: 1338–50.
- 100 Chiumello D, Chevillard G, Gregoretti C. Non-invasive ventilation in postoperative patients: a systematic review. *Intensive Care Med* 2011; **37**: 918–29.
- 101 Squadrone V, Cocha M, Cerutti E, et al. Continuous positive airway pressure for treatment of postoperative hypoxemia: a randomized controlled trial. *JAMA* 2005; **293**: 589–95.
- 102 Parke R, McGuinness S, Dixon R, Jull A. Open-label, phase II study of routine high-flow nasal oxygen therapy in cardiac surgical patients. *Br J Anaesth* 2013; **111**: 925–31.
- 103 Yu Y, Qian X, Liu C, Zhu C. Effect of high-flow nasal cannula versus conventional oxygen therapy for patients with thoracoscopic lobectomy after extubation. *Can Respir J* 2017; published online Feb 19. DOI:10.1155/2017:7894631.
- 104 Ansari BM, Hogan MP, Collier TJ, et al. A Randomized controlled trial of high-flow nasal oxygen (Optiflow) as part of an enhanced recovery program after lung resection surgery. *Ann Thorac Surg* 2016; **101**: 459–64.
- 105 Corley A, Bull T, Spooner AJ, Barnett AG, Fraser JF. Direct extubation onto high-flow nasal cannulae post-cardiac surgery versus standard treatment in patients with a BMI ≥ 30 : a randomised controlled trial. *Intensive Care Med* 2015; **41**: 887–94.
- 106 Futier E, Paugam-Burtz C, Godet T, et al. Effect of early postextubation high-flow nasal cannula vs conventional oxygen therapy on hypoxaemia in patients after major abdominal surgery: a French multicentre randomised controlled trial (OPERA). *Intensive Care Med* 2016; **42**: 1888–98.
- 107 Keenan SP, Powers C, McCormack DG, Block G. Noninvasive positive-pressure ventilation for postextubation respiratory distress: a randomized controlled trial. *JAMA* 2002; **287**: 3238–44.
- 108 Antonelli M, Conti G, Bui M, et al. Noninvasive ventilation for treatment of acute respiratory failure in patients undergoing solid organ transplantation: a randomized trial. *JAMA* 2000; **283**: 235–41.
- 109 Auriant I, Jallot A, Herve P, et al. Noninvasive ventilation reduces mortality in acute respiratory failure following lung resection. *Am J Respir Crit Care Med* 2001; **164**: 1231–35.
- 110 Jaber S, Delay JM, Chanques G, et al. Outcomes of patients with acute respiratory failure after abdominal surgery treated with noninvasive positive pressure ventilation. *Chest* 2005; **128**: 2688–95.
- 111 Jaber S, Lescot T, Futier E, et al. Effect of noninvasive ventilation on tracheal reintubation among patients with hypoxemic respiratory failure following abdominal surgery: a randomized clinical trial. *JAMA* 2016; **315**: 1345–53.
- 112 Futier E, Marret E, Jaber S. Perioperative positive pressure ventilation: an integrated approach to improve pulmonary care. *Anesthesiology* 2014; **121**: 400–08.
- 113 Kang BJ, Koh Y, Lim CM, et al. Failure of high-flow nasal cannula therapy may delay intubation and increase mortality. *Intensive Care Med* 2015; **41**: 623–32.
- 114 Carrillo A, Gonzalez-Diaz G, Ferrer M, et al. Non-invasive ventilation in community-acquired pneumonia and severe acute respiratory failure. *Intensive Care Med* 2012; **38**: 458–66.
- 115 Patel BK, Wolfe KS, Pohlman AS, Hall JB, Kress JP. Effect of noninvasive ventilation delivered by helmet vs face mask on the rate of endotracheal intubation in patients with acute respiratory distress syndrome: a randomized clinical trial. *JAMA* 2016; **315**: 2435–41.
- 116 Reynolds SC, Meyyappan R, Thakkar V, et al. Mitigation of ventilator-induced diaphragm atrophy by transvenous phrenic nerve stimulation. *Am J Respir Crit Care Med* 2017; **195**: 339–48.
- 117 Elkins M, Dentice R. Inspiratory muscle training facilitates weaning from mechanical ventilation among patients in the intensive care unit: a systematic review. *J Physiother* 2015; **61**: 125–34.